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Views on Biotechnology

George B. Rathmann
Amgen Inc.

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GEORGE B. RATHMANN

George B. Rathmann is President and Chief Executive Officer of Amgen Inc.

Introduction

Biotechnology is a most remarkable technology. I will present examples of the biotechnology revolution in widely diverse areas, including evidence that biotechnology is remaking the way the world discovers and develops pharmaceuticals and proof that the United States leads the world in this field. Then, I'll address the issues that have caused some to say that we should proceed slowly, cautiously, or possibly not at all. I'll comment on the questions of whether biotechnology is safe, wise, and moral and look at both the national and international perspectives.

This exciting story began in the 50s, when Watson and Crick said that the greatest impact of their elucidation of the double helical structure of DNA would be a rapidly growing understanding of all life processes. They correctly assessed the power of DNA and the importance of being able to understand its structure and manipulate DNA in the laboratory. How important is DNA to each of us? It turns out that these long molecules, which represent the blueprints of life are present in every living cell and the amount in each human being, if stretched end-to-end, would reach to the sun and back about 150 times. So there is a lot of DNA. An Amgen scientific advisory board member once stated that the elegance of DNA is that each cell contains sufficient information to be equivalent to about five encyclopedias. I accept that as a better definition of DNA. It surely is the most elegant matter in the universe.

Manipulating DNA permits us to use the mechanisms of living cells to make products. It might seem fairly limiting to only make things that are produced by living cells. But the extraordinary diversity of life makes it possible to make such simple molecules as alcohols and esters, acids and amino acids and then, through metabolic pathways, to make complicated enzymes, vitamins, proteins, and, of course, also to make DNA itself. So living cells have a great diversity, and the capability to harness DNA has ushered in the biotechnology revolution.

Where are the products of biotechnology produced? Not always, but very frequently in bacteria called *E. coli.* In the case of the product interferon, it is produced by the bacterium in such large quantities that the interferon is sequestered into little inclusion bodies, thereby helping partially purify the protein that we want to produce. The production of such a prodigious quantity of protein literally disables the bacterium to the point where it can no longer reproduce. As a result, we not only have to be able to insert the human interferon gene into the *E. coli,* we must also be able to turn the gene on at will. The bacteria must be allowed to multiply first.

This decade began with the announcement in January 1980 that Charles Weissman was successfully producing the wonder drug interferon in a bacterium (1). Interferon is only today, after seven years, beginning to live up to the great expectations of that time. However, the true significance of this announcement was that it stimulated the formation of many new companies that have helped establish the United States' leadership position. And, of course, in addition, there was an explosion of optimism about biotechnology.

Progress in Biotechnology to Date

Bioprocessing

One of the early promising potentials of biotech appeared to be in biomass conversion, to address the serious energy problems faced by the United States in the early 1980s when fuel prices rose. The thought of supplying simple chemicals by this new technology was very attractive, but the changes in oil prices from earlier projections made it uneconomical to try to make ethanol and other fuels through biotech. Such work, heavily subsidized, is still being done, and certainly will be important some time in the next century as the availability of fossil fuels diminishes.

The production of more complicated molecules via bioprocessing continues to offer exciting possibilities. An example of such bioprocessing is the production of indigo dye by bacterial cells. This capability was discovered accidentally when a scientist transferring a biochemical pathway from one bacteria into another noticed that his cells were turning blue. The two pathways had interacted to produce indigo, the dye used for blue jeans. (Indigo has been produced by synthetic organic chemicals for the past 100 years and was first isolated from plants more than 2,000 years ago.)

The exciting thing about bioprocessing is that it opens up the prospect of room temperature production of chemicals, not the cheapest ones, not the simple alcohols and acids, but more complicated chemicals that can be produced at room temperature without toxic catalysts, without toxic fumes, and without side reactions because biochemical processes can be highly specific. There is great potential for the production of a number of other molecules including vitamin C, other vitamins and enzymes. The first wave in the chemical field will be more complicated molecules than were originally envisioned, but very important products with significant environmental impact.

Agriculture

In the area of agriculture, a number of companies have shown that modified bacteria can improve the conversion of

nitrogen into the nitrates necessary for plant growth. When corn and other food crops can benefit from these advances, the reduction in the use of nitrate fertilizers that will be possible will have a profound environmental impact. In addition, plants have been genetically altered to resist insects or to have natural resistance to viruses and other pathogens. The impact of these developments is certainly going to be impressive, but the impact on the environment may be even more beneficial.

In summary, within the past six years genes have been introduced into plants to provide herbicide, insect, and pathogen resistance. The expression of the introduced genes can be controlled to produce the desired gene products. These genes are capable of being passed from generation to generation.

Animal Production and Health

In the areas of animal production and health, milk production has been increased safely in large numbers of animals, and improved meat quality is now possible. Recombinant vaccines have also been introduced for animals, and much progress has been made in general disease control.

For example, the administration of the hormone bovine somatotropin yields a 15-20% improvement in milk production for only a slight increase in feed. That is, the feed efficiency conversion to milk has been improved. Detection systems for determining how much administered somatotropin is in the milk show that the amount is essentially the same as is found in milk naturally; bovine somatotropin is a natural animal hormone that already exists in the cow.

In the case of pigs, the administration of porcine somatotropin produces a much leaner meat, a much healthier food, with again more efficient conversion from feed to meat. It is estimated that 50 million pigs will receive this product when it is approved.

This work has led people to speculate that soon we will have animals of weird shapes, designed to serve man and that we will forget about our responsibility to living things. However, I don't foresee a lot of chimeric animals. But, we should see the possibility of single cell proteins as a major source of protein for the world. Some big companies have bet on this already. Protein is produced with almost economic efficiency today in large containers that don't have any animals and these proteins don't even require sunlight. It's disease free, high quality protein. You can adjust the amino acid ratios to make sure the protein is perfect. However, it is not a food to which we are accustomed and it probably will take a long time to get accustomed to it. This type of food will happen before we have strange animals running around in the world; it is a safe and efficient way to meet humankind's nutritional needs.

Diagnostics

There has been great progress in diagnostics in the last six years. While monoclonal antibodies are not strictly speaking a product of recombinant DNA, they are certainly a product of advanced biotechnology. These very specific immunosystems provide specificity down to submolecular levels. Hybridization probes, which essentially use the binding action of DNA (exactly the same binding that holds the double helix together), have sensitivities down to 10^{-18} M. The long-range potential here is much earlier detection of disease so we can treat it when it is still treatable. The detection of diseases in the pre-natal stage or genetic screening may also be possible. Lastly, of course, the discovery of oncogenes and their link to cancer has given us new insights into that incredibly complex process and new cancer diagnostics are underway. Diagnostics are moving relatively rapidly now.

Pharmaceuticals

The major progress that has been most exciting to the world in the past several years has been in the pharmaceutical arena. Eight products are now marketed. All the targeted human proteins originally projected have been cloned, expressed, and produced at some level, including some very complex human proteins such as Factor VIII used to treat hemophilia. There are high expression (production levels) available so these materials can be produced practically, alleviating early concerns about whether enough product could be made. It turns out that for some of these materials one or two pounds will treat the world for a whole year.

Vaccines of a brand new type have been developed. They do not contain any of the pathogenic organism's DNA and cannot replicate. A problem of some conventional vaccines is sudden reversion and infection by the vaccine itself—no longer a risk with the new vaccines based on recombinant DNA. Here a little bit of the coat protein becomes the stimulus for the body's immune system and no pathogen is introduced at all. Magic bullets have been produced in which targeted antibodies carry toxins and destroy pathogenic cells. Major progress has been made in the past six years.

One of the exciting pharmaceuticals available, erythropoietin, is used to stimulate red blood cell production to combat certain forms of anemia. It takes about 20 micrograms or less per day of erythropoietin to restore normal red cell levels for many people, as compared to a maximum daily dose for things like Motrin or Tagamet of approximately two grams. When compared on a weight basis, erythropoietin is 100,000 times more potent, and on a molecular basis, it is 10 million times more potent. Therefore, we can use 1/10 millionth as many molecules to produce the therapeutic result. In addition, erythropoietin is a normal human protein which is exactly like, or very, very close to what is in the body already, and which has the metabolic pathways of products that already exist in our bloodstream. We are talking about a specificity so high that the probability of side effects is absolutely minimal. It is on this basis that it is clear that recombinant DNA affords a new way to produce pharmaceuticals.

A clinical study on erythropoietin, which has gone on now for a year and a half, indicates that there is a dose dependent response. Patients that were transfusion dependent can be taken off transfusions. There is no organ dysfunction, no antibody formation. The kind of data shown is some of the finest quantitative human data that has ever been seen with patient after patient showing responses in hematocrit level that increase very consistently depending upon the level of the drug administered. It is almost an idealized curve. Examining the case of a single patient is quite revealing. This patient had received 14 units of packed red cells in the previous 20 weeks. He was then placed on erythropoietin and given no more transfusions. The red blood cell level (the hematocrit of the patient) went up to normal. With transfusions this patient could not achieve above a 25 hematocrit, which is about 60% of normal. So we see a dramatic result from, again, microscopic quantities of these natural human proteins (2).

Two other products of biotechnology are tissue plasminogen activator or t-PA and granulocyte colony stimulating factor (G-CSF). Administration of t-PA can dissolve clots in coronary arteries interrupting a heart attack.

Treatment with G-CSF results in a large increase in white cells, largely neutrophils. This is exactly what the patient

needs in many cases. When cancer treatments destroy the body's ability to make white cells, the ones that disappear first, the neutrophils, are the cells that disarm the body's immune system. By restoring the body's neutrophils, we can bring patients back to normal. After a round of cancer chemotherapy, if the patient has been treated with G-CSF, studies on a small but meaningful number of patients indicate that the neutrophil level never drops below safe levels. The product looks very promising and it has a number of other applications in cancer therapy as well. G-CSF is perhaps one year behind erythropoietin in the extent of clinical studies completed and, of course, those will be necessary for final approval.

The exciting aspect of some of these highly directed therapies is the contrast they show to some of the earlier recombinant proteins that had broad responses but a wide spectrum of side effects. G-CSF and erythropoietin do not have the broad spectrum of response—each does only one thing, but it does it very well indeed. It does it without side effects.

Protein Engineering

An exciting new dimension of biotechnology that is still largely in the future is protein engineering. The concept here is that analogs to natural proteins can be made by altering the gene for that protein. We can take out a few segments of the gene and replace them with other segments. This is all straightforward molecular biology today. The net effect is that we can introduce new amino acids at will. The protein generated might look similar, or it might be that when the new unit is introduced the whole configuration assumes a very different shape. Most often if you introduce a new amino acid in a protein, its characteristics will be destroyed, but if you are very selective and do it in the right way, you can occasionally improve the product.

Scientists at Amgen took a somewhat different approach to protein engineering of alpha interferon. Recognizing that there are 14 kinds of alpha interferon and that a lot of homology or uniformity exists among the 14 types (see Figure 1), they concluded that nature was trying to make the concensus molecule. We averaged all of the 14 structures and produced that gene and its protein product. (Of course, with genetic engineering today, that is a very quick job. One can make the gene and produce the protein in a few weeks.) Our scientists found their product was, in fact, an active interferon, possibly five times more active than any of the 14 common ones. This protein is changed by 14 amino acids from all the others—a lot of amino acid changes—and yet has improved protein activity, a most unlikely event. It is obviously a very interesting product. It is now in advanced testing against viral diseases and it looks as if it will be a useful antiviral agent.

Results vs. Forecasts

Two years ago at an Industrial Research Institute Conference here in Minnesota, Paine Webber presented projections for market dates for eleven biologicals (Figure 2). I endorsed those figures. How well have our forecasts done? At that time projected marketing for alpha interferon was 1985-87; it went on the market in 1986 to treat one of the deadliest of cancers, hairy cell leukemia. From a market standpoint, a small market. From an importance standpoint, at least for the affected patients, it is life and death. Beta interferon has not been introduced yet, although there are some indications for antiviral activity. Also, there is hope that it has anti-cancer properties. It has been approved outside the United States but not here yet. Probably it will be marketed within those dates. For the product erythropoietin, 1990-1992 actually looks conservative. It could well be on the market in the very first part of that period, but then Food and Drug Administration (FDA) approval is not easy. The date projected for gamma interferon (1987-1989) may be a little early. Marketing could be later than 1989 because of the spectrum of responses the drug has had—it is very hard to identify where it fits in. In many cases, the side effects overwhelm the benefits. It is not clear that it will hit that date. Hepatitis B vaccine went on the market in 1986, earlier than projected. This vaccine is a very important contribution since 250 million people in the world are infected with that disease. They will not be helped by the vaccine, but future infections could be prevented.

Human growth hormone went on the market in 1985, and a second version of that hormone is going on the market right now; therefore, two products will be marketed by 1987. For interleukin-2, there were some very exciting early data (3), some more disappointing data (4), and then a reactivation of interest in this drug in recent publications in *The New England Journal of Medicine* (5, 6). It certainly looks as if it will be marketed by 1989, but not by 1987.

Monoclonal antibodies can target toxins, serving as magic bullets against cancer and magic bullets against infections. It is difficult to project market dates right now, but development appears to be on schedule.

Tissue plasminogen activator is definitely scheduled for this year. It could be the largest biotechnology product for many years to come.

Tumor necrosis factor is a complex biological response modifier with many effects other than just simply destroying tumors, which it does do. Balancing the side effects in human testing has not been achieved yet. But 1990-1991 is still a probable marketing date.

I'd like to assert and support the idea that the United States is leading the world in biotechnology. My view is largely the result of having traveled around the world and visited with all the other companies and noted the number of companies around the world that want Amgen to work with them. We have many relationships. There are more than 150 relationships between major Japanese companies and small U.S. biotechnology companies. I think that speaks clearly for where the Japanese think the Americans are. There is no doubt in our mind that the United States leads in this race. There is also no doubt that some of the commitments of other countries are very strong and that gap could close. Certainly it is a good time to address the balance of trade issues rather than wait until we're beaten and then try to restore balance by tariffs and other things. That is important to keep in mind. Other factors are much more important. The welfare of the people in this country. The benefits of these products here and around the world is certainly more important than just deciding we have a commitment to lead.

With two versions of alpha interferon, as well as insulin, human growth hormone, and the hepatitis B vaccine on the market and 30 more products in the development pipeline, the United States is well ahead in product development. Indeed each of these productss was introduced into clinical studies by U.S. firms.

Concerns about Biotechnology

Now let us consider some of the issues that have been raised about pursuing biotechnolgy, addressing the federal issues first. Arthur D. Little, a leading management and technology consulting firm, has suggested that there are some

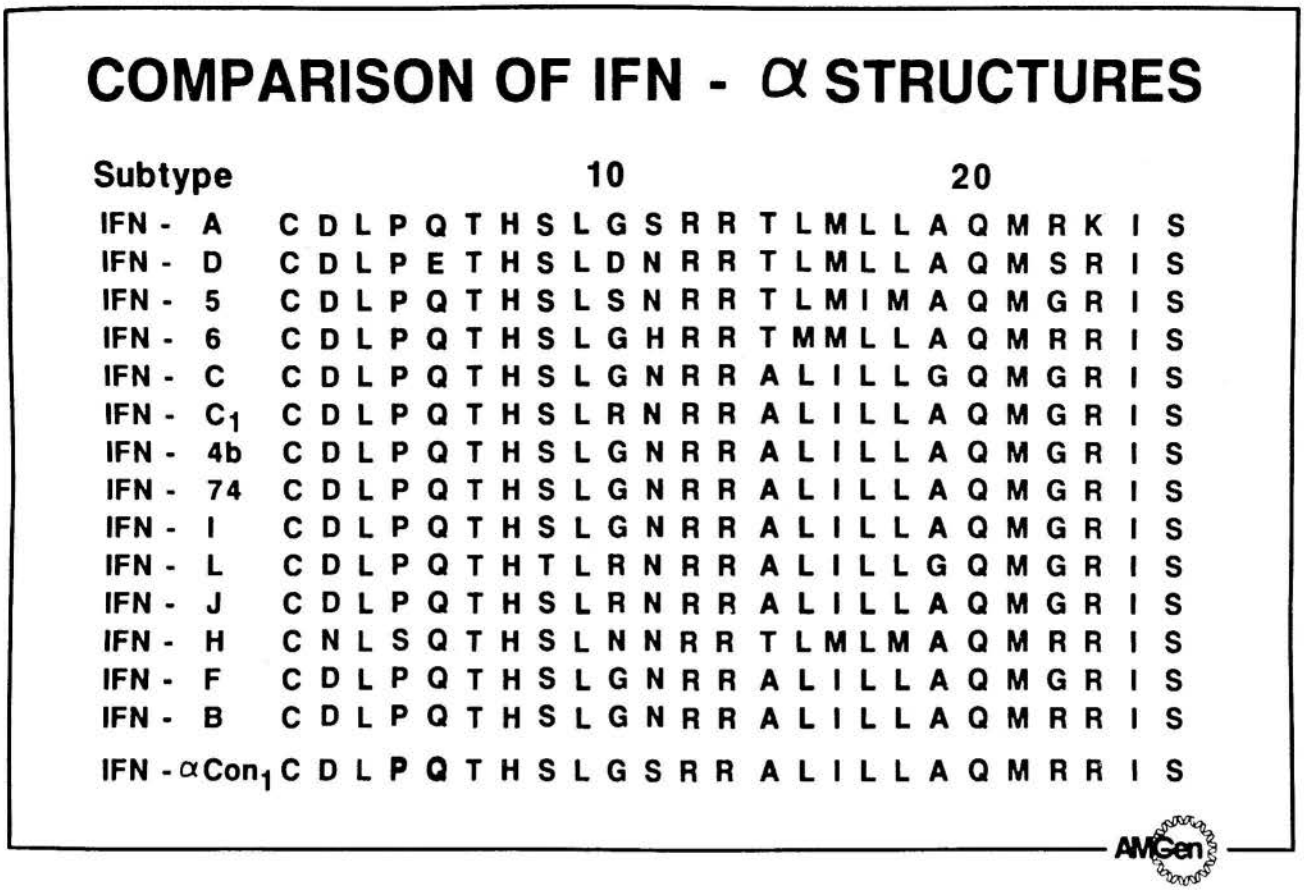


Figure 1. Comparison of the first 25 amino acids of the 14 naturally occurring forms of interferon. The bottom row is the consensus sequence generated by AMGen.

serious issues with respect to university and industry relationships, questioning whether we have perturbed the university's role (7). Actually, this concern was highlighted in 1981 by Robert Sinsheimer, in an address at the University of California, Santa Cruz, who said, "This spectacle of faculty seeking to exploit their research as private entrepreneurs is a scene fraught with conflicts of interest, destructive of collegiality, and erosive of the credibility of the university as a source of disinterested expertise" (8). Many were extremely concerned about this and we should be concerned and alert at all times about the change of the role of the university, which is so vital to our society. Our experience has been that although many leading academic people have affiliated themselves with biotech companies, we have never tried to control any of their publications. We don't review their publications and we don't fund programs dedicated to our interests. We have issued some grants, not many however, because of the fear that it might look as though we are trying to buy their research for us. I haven't noted any diminution in their dedication to their students or the principles of the promotion of science in this country.

Commercialization of biotechnology, of course, is the flip side of this. If we are going to promote it, how can we do it well? How can we do it safely? There is also the issue of risks. Are there risks? There must always be some. Let's make sure we're not glossing over them. Let's avoid secrecy at all costs. Let's respect the intellect of the American public and its ability to understand. Let's not decide what people don't know won't hurt them. Let's make sure they do understand these risks.

A number of recommendations for action concerning biotechnology policy have been suggested both by A.D. Little and others (7). U.S. leadership developed in the first place when federal support of research was coupled with the free enterprise of commercialization of biotechnology in small companies. Support of research should never be eliminated. The National Science Foundation (NSF) is going to double its budget in the next five years, but some biological research has not been growing as rapidly, or even been supported adequately, in the past couple of years. Supporting development sounds great. Let's do that too, but I am concerned that federal support of development may reduce the amount of research supported. Moreover, while research and development tax breaks sound great, a small company like ours didn't make money for four years. It really isn't a lot of help not to pay taxes when company losses mean no taxes are owed. While it is great for some companies, it doesn't really stimulate the growth of small companies, which I think is a very important goal.

Expedite patent action. There is a lot that could be said about the patent system. A lot of people don't understand it who should understand it. First, everybody associates the patent system with secrecy, while in fact, it has the opposite effect. You can keep a secret or you can patent it. When you patent it, you are going to file an application that represents the best embodiment of what you have. Our patents teach you exactly how to make our products. Within 18 months of the date we file those patent applications, they are published in full overseas and around the world. They are picked up by every country and by every other company. The unfortunate thing is that we are providing the information in exchange for patents, which are delayed for years and years because of the backlog in the Patent Office. I think the United States is disadvantaged in this regard. Creative companies are disadvantaged because they are providing the information and it is

PROJECTED MARKET DATES FOR 11 BIOLOGICALS

Product	Market Date	Company
Alpha Interferon	1985-1987	Biogen/Schering-Plough
		Genentech/Hoffmann-La Roche
		Amgen (Concensus alpha)
Beta Interferon	1987-1989	Cetus/Shell Oil
		Biogen/Schering-Plough
		Chiron/Lucky Ltd.
Erythropoietin	1990-92	Amgen/Kirin
		Genetics Institute
Gamma Interferon	1987-1989	Biogen
		Genentech/Boehringer/Daiichi
		Amgen
		Chiron/Lucky Ltd.

Source: Paine Webber

AMGen

PROJECTED MARKET DATES FOR 11 BIOLOGICALS

Product	Market Date	Company
Hepatitis B Vaccine	1987-1988	Merck/Chiron
		Biogen/Green Cross & Wellcome
		Amgen
Human Growth Hormone	1985-1986	Genentech/Kabi
Interleukin 2	1987-1989	Immunex/Hoffmann-La Roche
		Biogen
		Amgen
		Cetus
		Chiron
Monoclonal Antibody	1989-1991	Cetus
Anticancer Agents		Hybritech
		Xoma

Source: Paine Webber

AMGen

Figure 2. Projected market dates for 11 biologicals.

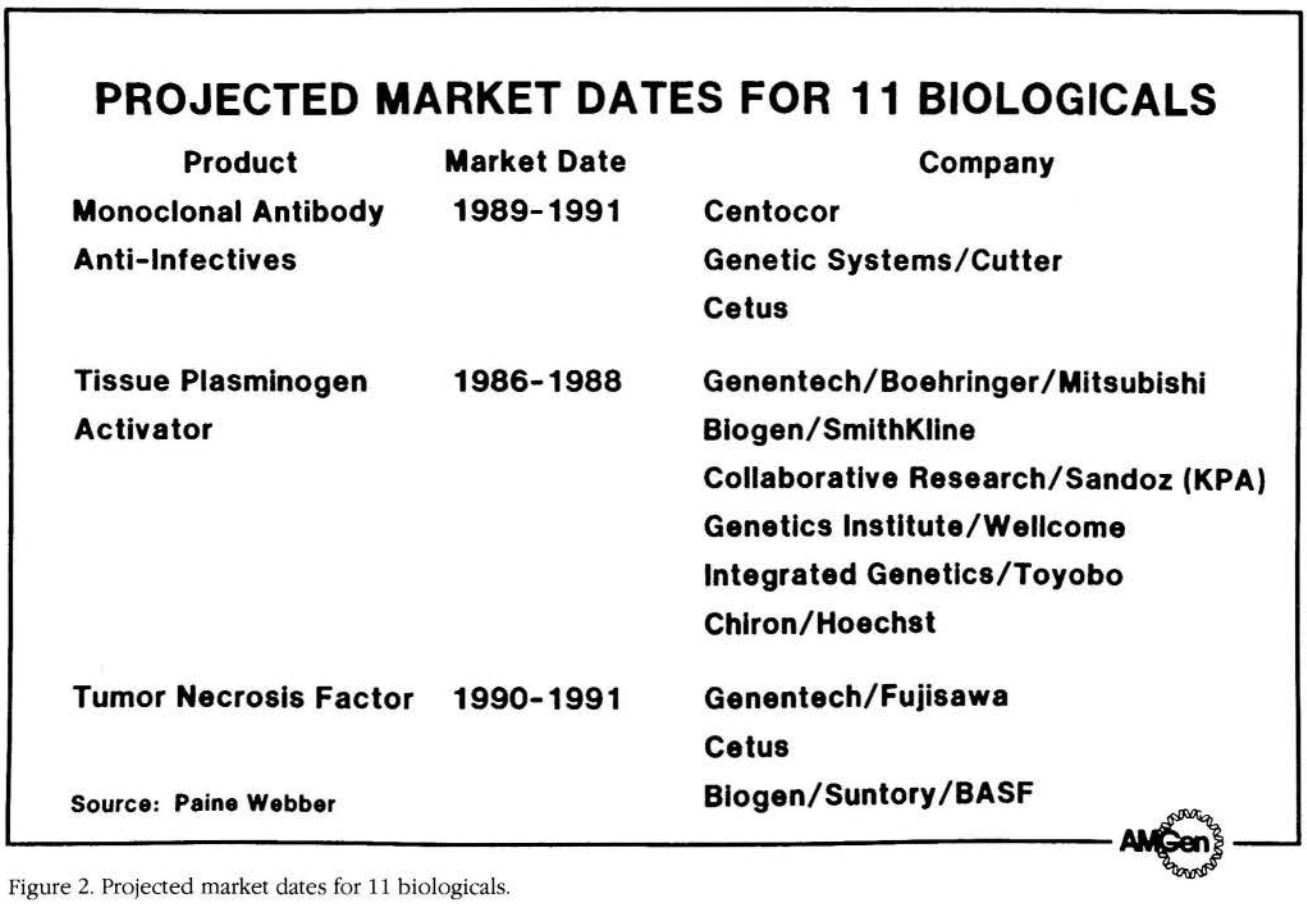


Figure 2. Projected market dates for 11 biologicals.

too long before the corresponding patent rights are awarded. Many people worry about whether it is right to patent things that are used to treat human beings. The motivation to create these products is that you are going to be able to market them under circumstances where not everybody is equal. It wasn't equal when you discovered them; why should you be equal in the marketplace. That is the basis of the patent system, which has stood the test of time for a couple of hundred years and is a fine system for encouraging creation and innovations. However, problems occur when it takes too long to get the protection that the disclosures justify.

People are interested also in expediting the regulatory process. There are always some fears when you say that—fears that we will have all sorts of disasters. However, when the regulatory process is so comprehensive that when you submit your documents to the FDA it may take a year to read them, you *know* there is something wrong with the process. The patients who are waiting for that drug could *never* comprehend taking two years to read the information that is going to make possible what they already know they want.

Figure 3 summarizes the roles of various federal agencies in biotech development and regulations. The regulatory process and whether the government is adequately involved is illustrated here in more than enough detail, indicating just how many parts of the government are involved in supporting or investigating, regulating, controlling, or agitating about biotechnology.

Probably the most controversial column on the chart indicates the Department of Defense's (DoD) interaction with biotech companies. Most of us have have a clear policy from the beginning. We have no secrets. We registered ourselves as a genetic engineering company in a community in California and we said if that is a concern to people, let's explain it to them. Let's not hide behind a different name. We've had no secrets. The DoD talked to us on one occasion. The ground rules they laid out was that we do not discuss biochemical or biological warfare, offensive or defensive. That was not going to come up. We had the discussion. We talked about things like erythropoietin and other materials. That is the only discussion our company has ever had. Some other companies, I am sure, have also had discussions. The government claims that it is not conducting offensive weapons research. We accept that. We certainly haven't. They are not doing any testing with us and I don't know of anybody with whom they are doing any. I think it has been of concern because secrecy is a deadly thing. When you don't hear about it, you don't know whether you're hearing everything or if something is being withheld. It is an issue.

However, the issue I was trying to highlight here is the incredible involvement of the government already. Efforts to try to simplify this usually scare us into thinking that we're probably going to end up with something more complicated. Largely, the system is working. I think it is well controlled. I think we're over-controlled to some degree and I think it's too slow, but I don't think we're badly in need of some overlay of additional and additional layers.

Hidden behind the question of how should the United States maintain its leadership in biotech, is an additional

FEDERAL AGENCY ACTIVITIES IN BIOTECHNOLOGY

Agency / Activities	FDA	USDA	DOD/ ONR	NIH	DOC	EPA	DOS	OSTP	NBS	OSHA	CDC	NASA	DOE	DOI	DOT	NSF	CRS
Commercialization	•	•		•	•	•	•	•								•	
Risk, Env. H&S			•	•		•				•							
Regulation	•	•				•											
Long Term					•	•											
International			•	•	•		•	•	•							•	
Coordination	•	•	•	•	•	•	•	•									
Innovation					•		•		•				•			•	
Liability						•											
Basic R&D	•	•	•	•		•			•		•	•	•			•	
Ethical				•													
Manpower & Training		•		•												•	

Figure 3. Activities of various federal agencies in the development and regulation of biotechnology (7).

question, *should* the United States maintain its leadership position in biotechnology? A survey by Monsanto (Figure 4) indicates there are some concerns out there (9). It is very important that we monitor these concerns, understand them, and try to have communication. Those surveyed were science policy leaders, environmental leaders, and religious leaders. Their most serious concern was the risk of creating undesirable organisms.

The surveyors also asked if the respondents believed that the benefits of biotechnology outweigh the risks. In fact, the science policy leaders feel so, the environmental leaders feel so with a little more ambivalence, and the religious leaders have major concerns. On the negative side, 27% of our religious leaders feel the risks outweigh the benefits. These are very important issues that should be addressed. Certainly if you feel the risks do outweigh the benefits, you shouldn't be trying to proceed and to maintain a leadership position in this field. We have some educating to do.

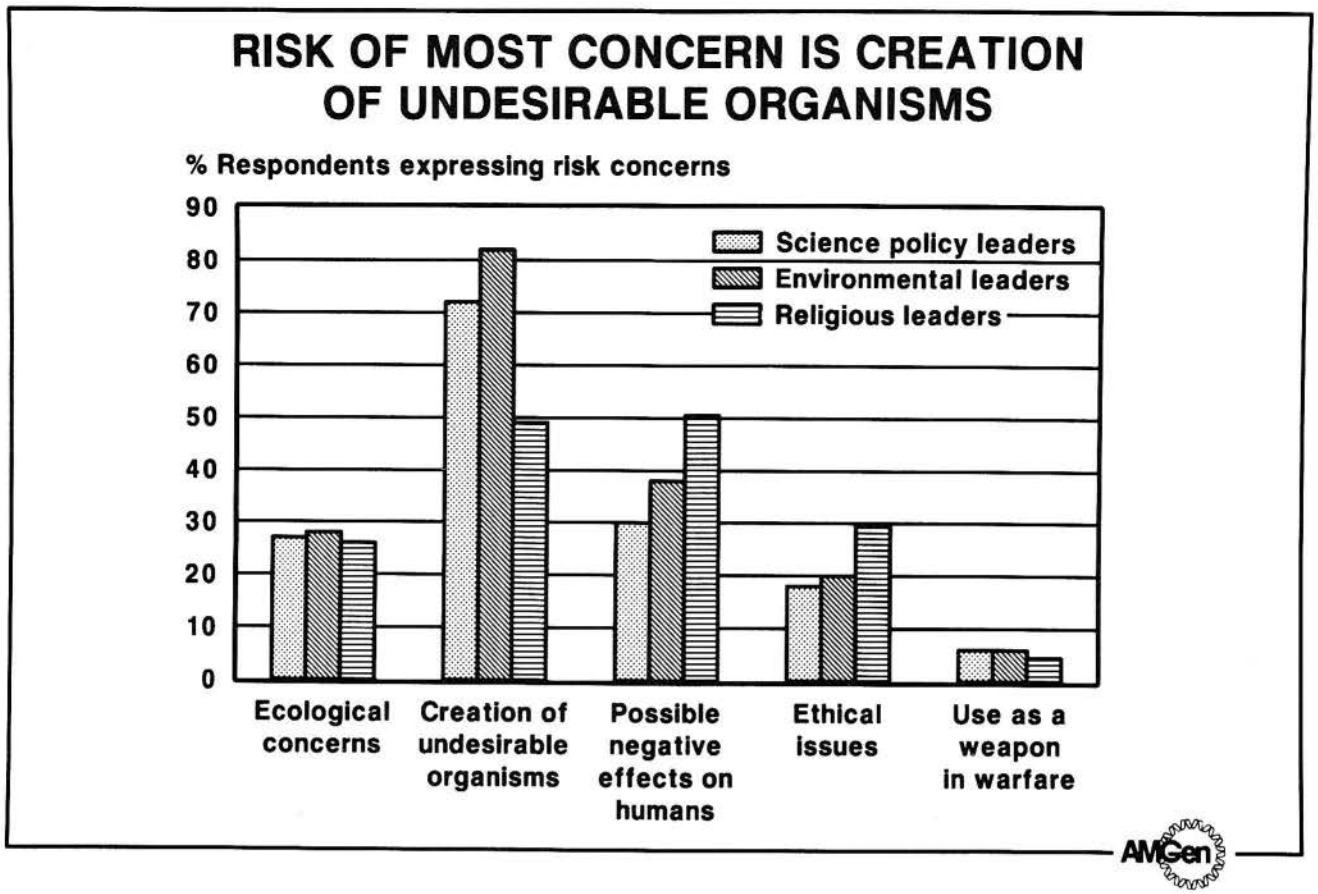
There are also others with great concerns. Eugene P. Odum says that enthusiasm for biotech should not lead us to treat all organisms merely as commodities for short-term gain (10). The long-term risk that he fears is undoubtedly ecological. What he seems to underestimate is the fact that many biotech products will reduce environmental stress and be used to detect and clean up some of the toxins we are already trying to eliminate.

Anthony Robbins, staff member on the Committee on Energy and Commerce, U.S. House of Representatives, says everything is going to go toward drain cleaners and cosmetics (11). My response to that is a list of vaccines that are in development for schistosomiasis, malaria, and for AIDS. There are more than a billion patients suffering from these diseases. Our hepatitis B vaccine has been tested in China where 1.8 million babies a year, two a minute, are being infected by hepatitis directly from their mothers. The vaccine works. It prevents that process. Biotechnology has made great progress and it is clear that Robbins is underestimating the application of this technology to do good.

Jeremy Rifkin, founder of the Foundation on Economic Trends and critic of genetic engineering, said, "Doesn't it make sense that we forestall biotechnology experiments until we've had a deep thorough national/international debate?" (12). He seems to think that will take a finite amount of time. We're concerned that the debate might well go on and although it might be a very important activity, it must go on in parallel with development if we wish to address the concerns of people who see biotechnology as having the best solution for their problems. Disease, nutrition, congenital defects, environment, aging, energy—they are all there to be dealt with and I don't think we can wait for the resolution of the total national/international debate.

Conclusion

In summary, biotechnology is solving problems with health, agriculture, and specialty chemicals. The United States



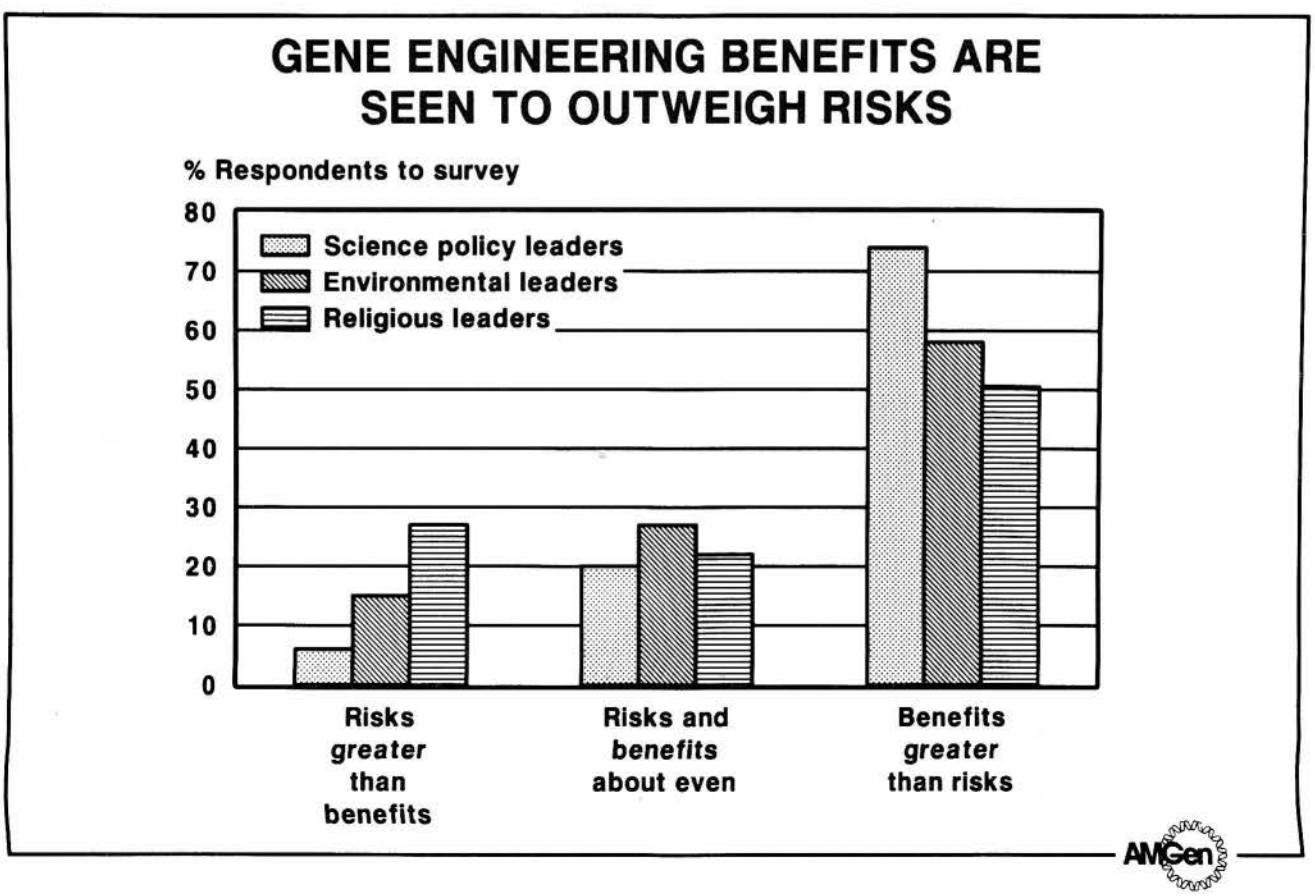


Figure 4. National survey of leaders in the fields of science policy, environmental issues, and religion on risks related to biotechnology. The survey was conducted by the Public Opinion Laboratory at Northern Illinois University and was sponsored by Monsanto (9).

leads in this development and really it is up to us to make sure that we get a broad enough understanding to maintain the support for this technology, to move it ahead with responsibility.

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Biotechnology: The Public Concerns

ROBERT L. SINSHEIMER

Robert L. Sinsheimer is Chancellor of the University of California at Santa Cruz.

Knowledge is power. Never has that been truer than in today's information age, with the exponential increase in human knowledge, with our ever more powerful computing devices, and with our extraordinary means of communication. "Give me a place to stand and I will move the earth," said Archimedes. Today we know that the place to stand is at the console of a supercomputer.

The other side of the coin, and there are always two sides, is to be found in Ecclesiastes; "He that increaseth knowledge, increaseth sorrow." The author of Ecclesiastes was not simply being morose or jaundiced. He knew that with increased knowledge inevitably comes increased responsibility, for good or for evil; together with the increased burden of decision; the wider potential for error; and the need for new ethical guidelines to define the boundaries of action in the new domain, wrested from the realm of innocence and ignorance.

Today we are at the verge of a most extraordinary advance in human knowledge, in the domain of the life sciences. We are about to achieve no less than a complete knowledge and understanding of the nature of life and the plan of evolution—and thereby of ourselves—as a part of life, a product of evolution.

The science of biology, in its continuing analysis of the processes of life, has penetrated to life's innermost secret—to the genes, to DNA, to the master programs that define the nature of each living cell and each living organism.

The genetic programs are carried on the chromosomes in the structure of very long DNA molecules. The DNA molecules are the well-known double helixes composed of a ladder of nucleotide pairs. There are four kinds of pairs and their sequence conveys the hereditary information. A gene is a tract of several hundred or several thousand such pairs and is located in a particular region on a particular chromosome.

We have already determined the complete genetic structure, the DNA sequence, of a few very simple organisms (up to 170,000 nucleotide pairs), and we now have the capacity and are setting out to determine the complete genetic structure of higher organisms and specifically, of man. A project is now being launched to sequence the entire human genome, some 3 billion nucleotide pairs of DNA. It can surely be done. It is only a matter of time and efficient approach (1).

This knowledge would permit a complete enumeration of the genetic ingredients of man. We estimate there are 100-300,000 genes in Homo sapiens. These will now be defined and enumerated.